Tissue engineering: construction of a multicellular 3D scaffold for the delivery of layered cell sheets.

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Public Summary:
Many tissues, such as the adult human hearts, are unable to adequately regenerate after damage.(2,3) Strategies in tissue engineering propose innovations to assist the body in recovery and repair. For example, TE approaches may be able to attenuate heart remodeling after myocardial infarction (MI) and possibly increase total heart function to a near normal pre-MI level.(4) As with any functional tissue, successful regeneration of cardiac tissue involves the proper delivery of multiple cell types with environmental cues favoring integration and survival of the implanted cell/tissue graft. Engineered tissues should address multiple parameters including: soluble signals, cell-to-cell interactions, and matrix materials evaluated as delivery vehicles, their effects on cell survival, material strength, and facilitation of cell-to-tissue organization. Studies employing the direct injection of graft cells only ignore these essential elements.(2,5,6) A tissue design combining these ingredients has yet to be developed. Here, we present an example of integrated designs using layering of patterned cell sheets with two distinct types of biological-derived materials containing the target organ cell type and endothelial cells for enhancing new vessels formation in the "tissue". Although these studies focus on the generation of heart-like tissue, this tissue design can be applied to many organs other than heart with minimal design and material changes, and is meant to be an off-the-shelf product for regenerative therapies. The protocol contains five detailed steps. A temperature sensitive Poly(N-isopropylacrylamide) (pNIPAAM) is used to coat tissue culture dishes. Then, tissue specific cells are cultured on the surface of the coated plates/micropattern surfaces to form cell sheets with strong lateral adhesions. Thirdly, a base matrix is created for the tissue by combining porous matrix with neovascular permissive hydrogels and endothelial cells. Finally, the cell sheets are lifted from the pNIPAAM coated dishes and transferred to the base element, making the complete construct.

Scientific Abstract:
Many tissues, such as the adult human hearts, are unable to adequately regenerate after damage.(2,3) Strategies in tissue engineering propose innovations to assist the body in recovery and repair. For example, TE approaches may be able to attenuate heart remodeling after myocardial infarction (MI) and possibly increase total heart function to a near normal pre-MI level.(4) As with any functional tissue, successful regeneration of cardiac tissue involves the proper delivery of multiple cell types with environmental cues favoring integration and survival of the implanted cell/tissue graft. Engineered tissues should address multiple parameters including: soluble signals, cell-to-cell interactions, and matrix materials evaluated as delivery vehicles, their effects on cell survival, material strength, and facilitation of cell-to-tissue organization. Studies employing the direct injection of graft cells only ignore these essential elements.(2,5,6) A tissue design combining these ingredients has yet to be developed. Here, we present an example of integrated designs using layering of patterned cell sheets with two distinct types of biological-derived materials containing the target organ cell type and endothelial cells for enhancing new vessels formation in the "tissue". Although these studies focus on the generation of heart-like tissue, this tissue design can be applied to many organs other than heart with minimal design and material changes, and is meant to be an off-the-shelf product for regenerative therapies. The protocol contains five detailed steps. A temperature sensitive Poly(N-isopropylacrylamide) (pNIPAAM) is used to coat tissue culture dishes. Then, tissue specific cells are cultured on the surface of the coated plates/micropattern surfaces to form cell sheets with strong lateral adhesions. Thirdly, a base matrix is created for the tissue by combining porous matrix with neovascular permissive hydrogels and endothelial cells. Finally, the cell sheets are lifted from the pNIPAAM coated dishes and transferred to the base element, making the complete construct.